

- d) compounds which inhibit or activate expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- e) delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which target cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,

delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which are targeted to the endothelium and induce necrosis or apoptosis.

11. (Amended) Pharmaceutical compositions according to claim 1 which comprise as compound II at least one of

- f) compounds which inhibit receptor tyrosine kinase activity,
- g) compounds which inhibit ligand binding to receptors,
- h) compounds which inhibit activation of intracellular signal pathways of the receptors,
- i) compounds which inhibit or activate expression of a ligand or of a receptor of the VEGF or Tie receptor system,
- j) delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which target cytotoxic agents or coagulation-inducing agents to the endothelium via recognition of VEGF/VEGF receptor or Angiopoietin/Tie receptor systems,

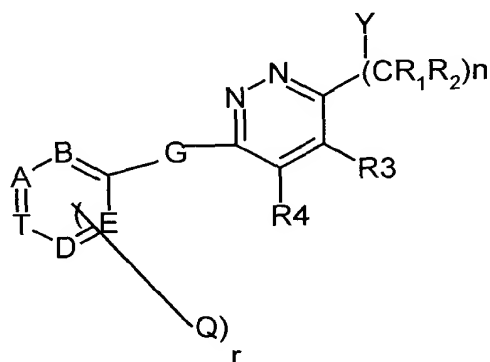
delivery systems, such as antibodies, ligands, high-affinity binding oligonucleotides or oligopeptides, or liposomes, which are targeted to the endothelium and induce necrosis or apoptosis.

12. (Amended) Pharmaceutical compositions according to claim 1 which comprise as compound I and/ or II at least one of Seq. ID Nos. 1-59.

~~13. (Amended) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II Seq. ID Nos. 34a.~~

14. (Amended) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II at least one of sTie2, mAB 4301-42-35, scFv-tTF and/or L19 scFv-tTFconjugate.

15. (Amended) Pharmaceutical compositions according to claim 1 which comprise as compound I and/or II at least one small molecule of general formula I



I,

in which

r has the meaning of 0 to 2,

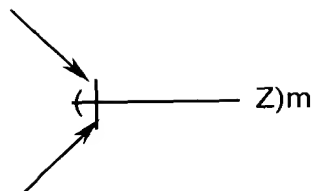
n has the meaning of 0 to 2;

R₃ und R₄

a) each independently from each other have the meaning of lower alkyl,

b) together form a bridge of general partial formula

II,



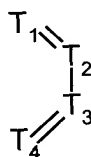
II,

wherein the binding is via the two terminal C- atoms,

and

has the meaning of 0 to 4; or

c) together form a bridge of partial formula III



III,

wherein one or two of the ring members $\text{T}_1, \text{T}_2, \text{T}_3, \text{T}_4$ has

the meaning of nitrogen, and each others have the

meaning of CH, and the bining is via the atoms T_1 and

T_4 ;

G has the meaning of C_1 - C_6 - alkyl, C_2 - C_6 - alkylene or

C_2 - C_6 - alkenylene; or C_2 - C_6 - alkylene or C_3 - C_6 -

alkenylene, which are substituted with acyloxy or

hydroxy; $-\text{CH}_2\text{-O-}$, $-\text{CH}_2\text{-S-}$, $-\text{CH}_2\text{-NH-}$, $-\text{CH}_2\text{-O-CH}_2\text{-}$,

$-\text{CH}_2\text{-S-CH}_2\text{-}$, $-\text{CH}_2\text{-NH-CH}_2\text{-}$, oxa ($-\text{O-}$), thia ($-\text{S-}$) or

imino ($-\text{NH-}$),

A, B, D, E and T independently from each other have the meaning of N or CH, with the proviso that not more than three of these Substituents have the meaning of N,

Q has the meaning of lower alkyl, lower alkyloxy or halogene,

R₁ and R₂ independently from each other have the meaning of H or lower alkyl,

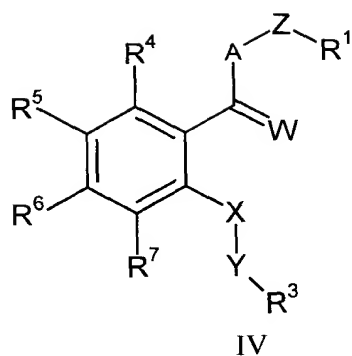
X has the meaning of imino, oxa or thia;

Y has the meaning of hydrogen, unsubstituted or substituted aryl, heteroaryl, or unsubstituted or substituted cycloalkyl; and

Z has the meaning of amino, mono- or disubstituted amino, halogen, alkyl, substituted alkyl, hydroxy, etherificated or esterificated hydroxy, nitro, cyano, carboxy, esterificated carboxy, alkanoyl, carbamoyl, N-mono- or N, N- disubstituted carbamoyl, amidino, guanidino, mercapto, sulfo, phenylthio, phenyl-lower-alkyl-thio, alkyl-phenyl-thio, phenylsulfinyl, phenyl-lower-alkyl-sulfinyl, alkylphenylsulfinyl, phenylsulfonyl, phenyl-lower-alkan-sulfonyl, or alkylphenylsulfonyl,

whereas, if more than one rest Z is present ($m \geq 2$), the substituents Z are equal or different from each other,

and wherein the bonds marked with an arrow are single or double bonds; or an N-oxide of said compound, wherein one or more N-atoms carry an oxygene atom, or a salt thereof, and/or a compound of general formula IV

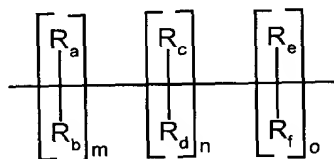


in which

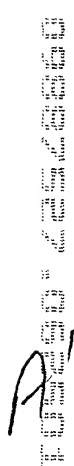
A has the meaning of group $=NR^2$,

W has the meaning of oxygen, sulfur, two hydrogen atoms or the group $=NR^8$,

Z has the meaning of the group $=NR^{10}$ or $=N-$, $-N(R^{10})-(CH_2)_q-$, branched or unbranched C_{1-6} -Alkyl or is the group



or A, Z and R^1 together form the group



has the meaning of 0 – 3,

has the meaning of 1 – 6,

independently from each other have the meaning of hydrogen, C₁₋₄ alkyl or the group =NR¹⁰, and/ or R_a and/ or R_b together with R_c and or R_d or R_c together with R_e and/ or R_f form a bound, or up to two of the groups R_a-R_f form a bridge with each up to 3 C-atoms with R¹ or R²,

has the meaning of group =NR⁹ or =N-,

has the meaning of group $-(\text{CH}_2)_p$,

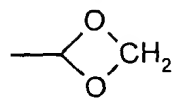
has the meaning of integer 1-4,

has the meaning of unsubstituted or optionally substituted with one or more of halogene, C₁₋₆-alkyl, or C₁₋₆-alkyl or C₁₋₆-alkoxy, which is optionally substituted by one or more of halogen, or is unsubstituted or substituted aryl or heteroaryl,

R³ has the meaning of monocyclic or bicyclic aryl or heteroaryl which is unsubstituted or optionally substituted with one or more of
für halogen, C₁₋₆-alkyl, C₁₋₆-alkoxy or hydroxy,

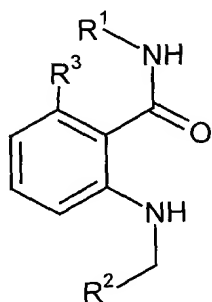
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or more of halogene, or R⁵ and R⁶ together form the group



R⁸, R⁹ and R¹⁰ independently from each other have the meaning of hydrogen or C₁₋₆-alkyl, as well as their isomers and salts,

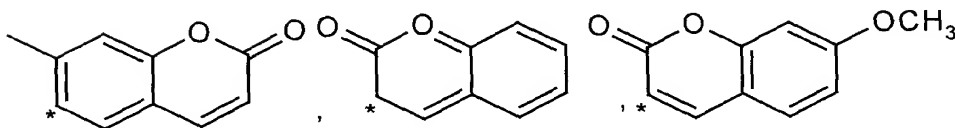
and/ or a compound of general formula V

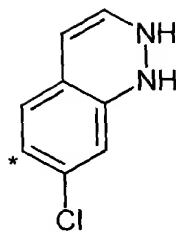
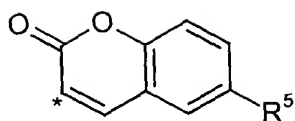


V,

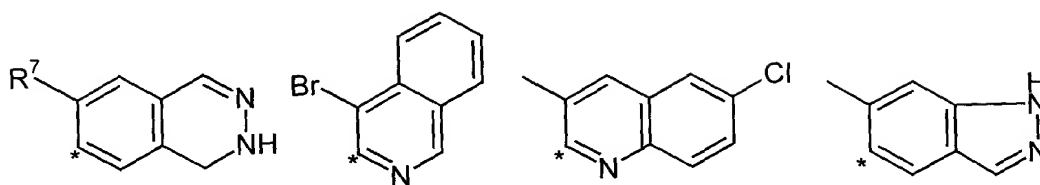
in which

R¹ has the meaning of group

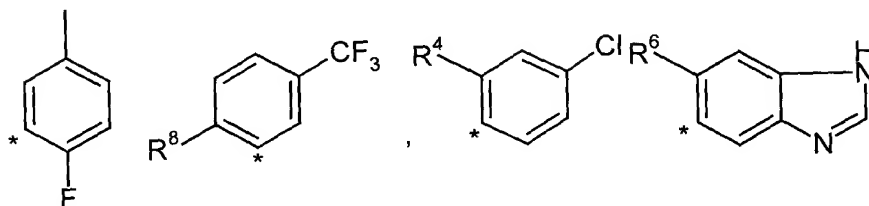




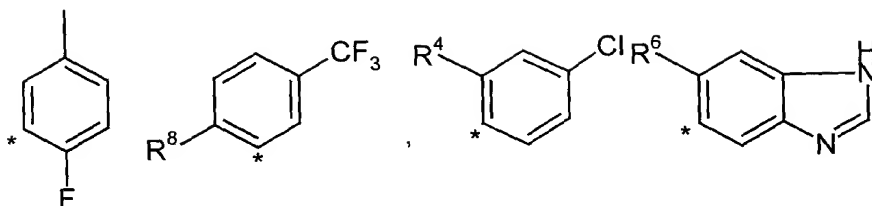
in which R^5 is chloro, bromo or the group $-OCH_3$,



in which R^7 is $-CH_3$ or chloro,



in which R^7 is $-CH_3$ or chloro,

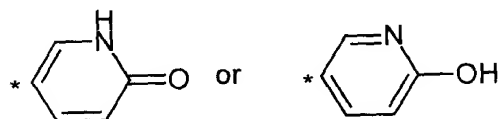


in which R^8 is $-CH_3$, fluoro, chloro or $-CF_3$

in which R^4 is fluoro, chloro, bromo, $-CF_3$, $-N=C$, $-CH_3$, $-OCF_3$ or $-CH_2OH$

in which R^6 is $-CH_3$ or chloro

R^2 has the meaning of pyridyl or the group



and

R^3 has the meaning of hydrogen or fluoro, as well as their isomers and salts.

17. (Amended) Pharmaceutical compositions according to claims 1-16 which comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, and as compound II (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate, sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate, with the proviso that compound I is not identically to compound II.

18. (Amended) Pharmaceutical compositions according to claims 1-17 which

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comprise as compound I (4-Chlorophenyl)[4-(4-pyridylmethyl)-phthalazin-1-yl]ammonium hydrogen succinate and as compound II sTie2, mAB 4301-42-35, scFv-tTF and/ or L19 scFv-tTF conjugate.

19. (Amended) Pharmaceutical compositions according to claims 1-17 which comprise as compound I mAB 4301-42-35 and as compound II sTie2, and/ or scFv-tTF conjugate.

20. (Amended) Pharmaceutical compositions according to claims 1-17 which comprise as compound I scFv-tTF conjugate and as compound II sTie2 and/ or mAB 4301-42-35.

21. (Amended) Pharmaceutical compositions according to claims 1-17 which comprise as compound I L19 scFv-tTF conjugate and as compound II sTie2.

22. (Amended) Use of pharmaceutical compositions according to claims 1-21, for the production of a medicament for the treatment of tumors, cancers, psoriasis, arthritis, such as rheumatoid arthritis, hemangioma, angiofibroma, eye diseases, such as diabetic retinopathy, neovascular glaucoma, kidney diseases, such as glomerulonephritis, diabetic nephropathy, malignant nephrosclerosis, thrombotic microangiopathic syndrome, transplantation rejections and glomerulopathy, fibrotic diseases, such as cirrhotic liver, mesangial cell proliferative diseases, arteriosclerosis, damage of nerve tissues, suppression of the ascites formation in patients and suppression of VEGF oedemas.